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Stability of the acoustic startle reflex, prepulse inhibition, and habituation in schizophrenia

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Abstract

Prepulse inhibition (PPI) of the acoustic startle reflex has been proposed as a neurophysiological measure of sensorimotor gating. There is high test–retest reliability of both startle magnitude and PPI in non-psychiatric subjects. The present study examined the stability of the acoustic startle reflex and its modulation in patients with schizophrenia. Startle measurements were performed in 19 chronic schizophrenic patients on stable medications and 24 healthy control subjects, three times at one-month intervals. PPI trials with various intervals between the prepulse and the startle stimulus (30, 60, 120, 240, and 2000 ms) were used. Intraclass correlation coefficients (ICC) were computed to assess stability. There was a good test–retest reliability of PPI in both schizophrenic patients (Mean ICC: 0.75) and control subjects (Mean ICC: 0.71). Acoustic startle magnitude was the most stable measure across sessions (Mean ICC schizophrenics: 0.89; Mean ICC controls: 0.89). In both groups, a good test–retest reliability was found in the startle latencies. Habituation and prepulse-induced shortening of latencies exhibited moderate stability. Schizophrenic patients exhibited significantly less PPI than control subjects in the 60 ms prepulse condition. This PPI deficit was evident in all three sessions. These results indicate that PPI is a stable neurobehavioral measure in chronic schizophrenic patients in the absence of changes in clinical state. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

The acoustic startle reflex is a contraction of the skeletal musculature in response to an intense acoustic stimulus, typically measured by electromyography (EMG) of the musculus orbicularis oculi. Prepulse inhibition (PPI) refers to the inhibition of the startle reflex by a weak prepulse presented prior to the startling stimulus. This modulation of the startle reflex has been proposed as a neurophysiological measure

of sensorimotor gating (Braff and Geyer, 1990; Geyer et al., 1990; Swerdlow et al., 1994) regulated by forebrain cortico–striato–pallido–pontine neural circuitry (Braff and Geyer, 1990; Swerdlow et al., 1992). In particular, PPI deficits and deficits in habituation of the startle reflex have been quantified in schizophrenic patients (Braff et al., 1978, 1992, 1995; Geyer and Braff, 1982; Grillon et al. 1992; Bolino et al., 1994). There have also been reports of PPI deficits in schizotypal (Cadenhead et al., 1993) patients and psychosis-prone persons (Simons and Giardina, 1992; Swerdlow et al., 1995). In this context, PPI and startle habituation have been suggested to be trait-linked markers of vulnerability to schizophrenia spectrum disorders

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(Braff, 1993; Cadenhead et al., 1993). To evaluate the startle reflex and its modulation as a trait marker, it is important to assess the test–retest reliability of these measures across time in schizophrenic patients.

The stability of PPI over time has been examined in non-psychiatric populations. Braff et al. (1978) first reported moderate stability of startle magnitude between two sessions at a 10-day interval. In a design with three sessions and 1-week intervals, Schwarzkopf et al. (1993) used intraclass correlations (ICCs) to demonstrate the stability of both PPI and startle magnitudes. Similarly, Cadenhead et al. (1999) reported high ICCs for PPI, habituation, startle magnitude, startle latency and latency facilitation across three sessions at monthly intervals. On a shorter time scale, Abel et al. (1998) found good test–retest reliability of PPI, habituation, and startle magnitude across three sessions within one day.

To date, stability of the startle reflex and its modulation have not been examined in schizophrenic patients. Accordingly, the present study examined the test–retest reliability of PPI, startle magnitude, habituation, peak latency, and latency facilitation in schizophrenic patients and healthy control subjects across three sessions at monthly intervals. Additionally, we assessed differences in startle measures between the two groups.

2. Methods

2.1. Subjects

Twenty-four patients with a DSM-IV (American Psychiatric Association, 1994) diagnosis of schizophrenia were recruited through the Inpatient Psychiatric Services of Aargau Canton (Switzerland). The 27 control subjects were hospital employees or were recruited through local advertisements. Because of unusable eye-blink data, three patients and three controls were excluded from the final analyses. Two patients chose not to continue the study after the first session. After these exclusions, the schizophrenic group ($N = 19$) consisted of 15 men and 4 women with a mean ($\pm$SD) age of 42 ± 9 years (range 29–58 years). DSM-IV diagnosis (American Psychiatric Association, 1994) was based on an individual semi-structured psychiatric interview by an experienced

Table 1
Clinical characteristics of schizophrenic patients ($n = 19$), CGI, PANSS, SCL-90

Scale	Characteristic	Mean	SD
CGI	CGI — session 1	5.6	0.7
	CGI — session 2	5.8	0.7
	CGI — session 3	5.6	0.6
PANSS	Positive symptoms	16.8	5.5
	Negative symptoms	22.4	4.5
	General psychopathology	44.1	7.3
SCL-90	Global severity index	1.3	0.7

clinician. The mean duration of illness was 21 ± 10 years (range 5–41 years). All patients showed a chronic disease process and lived in a long-term treatment facility. Fifteen patients met the criteria for a paranoid subtype of schizophrenia, two for a residual subtype, and two for an undifferentiated subtype. All patients received a stable dose of antipsychotic medication throughout the investigation, with a mean chlorpromazine equivalent of 495.3 ± 382.1 mg (range: 140–1667 mg). Eleven patients received typical antipsychotics, six atypical, and two a combination of both. During each session, symptoms were rated with the Positive and Negative Syndrome Scale Score (PANSS; Kay et al., 1987), the Clinical Global Impression (CGI; Guy, 1976) and the Symptom Check List (SCL-90; Derogatis, 1977). Table 1 presents relevant clinical characteristics of the patients. The semi-structured interview in the control group revealed no personal history of psychiatric disorder, substance abuse, or major medical disorder as well as the absence of psychosis in first-degree relatives. After exclusion of subjects with unusable startle data ($n = 3$), the control group ($n = 24$) consisted of 14 men and 10 women with a mean age of 30 ± 10 years (range 20–55 years). The control subjects also had to complete the SCL-90 during each session (mean global severity index 0.3 ± 0.4). Women were tested in the early follicular phase of their menstruation cycle because PPI has been shown to be most robust at this time (Swerdlow et al., 1996). After complete description of the study to the subjects, written informed consent was obtained. All patients and control subjects were tested three times at 1-month intervals, by the same investigator and under the same conditions.